K121461

BIOMÉRIEUX

JAN 2 2 2013

510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Name of device

BacT/ALERT® FA Plus

Device Identification

Trade Name: BacT/ALERT® FA Plus Culture Bottle
Classification Name: Blood Culturing System, Microbiology
Product Code: MDB
Regulation: 21CFR866.2560, microbial growth monitor
Device Class: Class 1, not exempt from premarket notification per 21CFR807.81

Premarket Notification Submitter

Company Name:	bioMérieux, Inc.
Company Address:	100 Rodolphe Street Durham, NC 27712
Contact:	Jocelyn Jennings, Senior Manager, Regulatory Affairs
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Preparation Date:	May 16, 2012

Intended Use of the Device

BacT/ALERT® FA Plus Culture Bottles are used with the BacT/ALERT® Microbial Detection System in qualitative procedures for enhanced recovery and detection of aerobic and facultative anaerobic microorganisms (bacteria and yeast) from blood and other normally sterile body fluids.

Description of the Device

The new reagent (BacT/ALERT FA Plus Culture Bottle) is an improvement upon the cleared charcoal formulation reagent (BacT/ALERT FA Culture Bottle). The BacT/ALERT FA Culture Bottles are used with the BacT/ALERT Microbial Detection Systems in qualitative procedures for recovery and detection of microorganisms from blood.

The predicate BacT/ALERT FA Culture Bottle contains charcoal, for its antimicrobial neutralization properties, in a complex growth medium. Charcoal

is eliminated in the proposed BacT/ALERT FA Plus Culture Bottle, and is replaced with two types of adsorbent resins in a complex growth medium. The proposed BacT/ALERT FA Plus Culture Bottle is optimized to increase antimicrobial neutralization properties, and to increase the clarity of Gram stains in comparison to the predicate BacT/ALERT FA Culture Bottle.

The BacT/ALERT Microbial Detection System provides both a microbial detection system and a culture medium bottle with suitable nutritional and environmental conditions for microorganisms commonly encountered in blood or other normally sterile body fluid samples (except urine) taken from a patient suspected of having bacteremia/fungemia. An inoculated bottle is placed into the instrument where it is incubated and continuously monitored for the presence of microorganisms that will grow in the BacT/ALERT bottles.

The BacT/ALERT Microbial Detection System utilizes a colorimetric sensor and reflected light to monitor the presence and production of carbon dioxide (CO_2) that is dissolved in the culture medium. If microorganisms are present in the test sample, carbon dioxide is produced as the microorganisms metabolize the substrates in the culture medium. When growth of the microorganisms produces CO_2, the color of the gas-permeable sensor installed in the bottom of each culture bottle changes from blue-green to yellow. The lighter color results in an increase of reflectance units monitored by the system. Bottle reflectance is monitored and recorded by the instrument every 10 minutes.

SUBSTANTIAL EQUIVALENCE INFORMATION

Predicate device name(s):

BacT/ALERT® FA Culture Bottle

Predicate device 510(k) number(s)

K020813

Comparison with predicate

The BacT/ALERT FA Plus Culture Bottle is claimed substantially equivalent to the BacT/ALERT FA Culture Bottle (**K020813**).

Table 1. Similarities and differences between the tests are outlined below:

Culture Bottle Characteristics: Changes versus K020813	
Specimen Sampling and Handling	unchanged
Assay Types	unchanged
Reaction Types	unchanged
Calibration	unchanged
Quality Control (by Operator)	unchanged
Principles of Operation	unchanged
Firmware	No changes to firmware code occurred. The structure of the firmware algorithm remain unchanged. The knowledge base specifications utilized by the firmware included changes to the initial value threshold variables used by the firmware algorithm. Variables related to controlling barcode recognition were adjusted to enable recognition of the new bottle type.

Performance Characteristics

Analytical Testing

Analytical Sensitivity: Growth Performance

Data represent results from in-house seeded studies with and without blood obtained from healthy human volunteers. Multiple strains were tested for each species at target inoculum levels of 125 CFU per bottle. The species listed are representatives of clinically prevalent organisms in blood cultures and sterile body fluids.

Table 2. Growth Performance Results

Microorganism	Blood				No Blood			
	% Recovery (n)	Range CFU/bottle	Time to Detection (hours)		% Recovery* (n=3)	Range CFU/bottle	Time to Detection (hours)	
			Mean	Range			Mean	Range
Staphylococcus aureus	100.0 (33/33)	54 - 150	13.4	12.2 - 15.6	100	116 - 150	16.7	14.6 - 18.2
Escherichia coli	100.0 (33/33)	71 - 254	11.3	10.3 - 12.4	100	73 - 176	11.4	10.6 - 11.9
Pseudomonas aeruginosa	100.0 (15/15)	74 - 148	16	13.7 - 18.6	100	74 - 148	20.8	17.8 - 25.6
Klebsiella pneumoniae	100.0 (15/15)	89 - 123	11.3	10.6 - 12.3	100	95 - 123	12	11.6 - 12.4
Candida albicans	100.0 (38/38)	88 - 298	28.9	19.2 - 52.8	100	88 - 298	27.1	22.1 – 30.1
Streptococcus pneumoniae	100.0 (33/33)	3 - 260	13.9	10.8 - 16.5	100	4 - 25	14.3	13.01 - 16.3

Microorganism	Blood				No Blood			
	% Recovery (n)	Range CFU/bottle	Time to Detection (hours)		% Recovery* (n=3)	Range CFU/bottle	Time to Detection (hours)	
			Mean	Range			Mean	Range
Staphylococcus epidermidis	100.0 (15/15)	44 - 135	17.6	14.3 - 36.0	100	45 - 105	21.4	19.0 - 24.8
Enterococcus faecalis	100.0 (15/15)	63 - 259	11.6	11.0 - 12.3	100	71 - 169	12.3	11.8 - 12.7
Enterococcus faecium	100.0 (15/15)	25 - 120	12.6	11.3 - 14.4	100	25 - 120	15.5	14.0 - 17.5
Enterobacter cloacae	100.0 (15/15)	111 - 200	12	10.8 - 15.7	100	111 - 185	11.7	11.3 - 12.0
Candida glabrata	100.0 (15/15)	118 - 281	44.8	27.3 - 64.8	100	118 - 194	39.9	30.9 - 50.4
Haemophilus influenzae	100.0 (15/15)	105 - 266	14.4	12.1 – 16.8	0	-	-	-
Proteus mirabilis	100.0 (15/15)	36 - 213	12.9	11.3 - 16.3	100	36 - 213	12.5	11.3 - 13.6

*In case of less than 100% recovery, it is recommended to add blood such as sterile defibrinated horse blood (10% v/v).[3]

Antimicrobial Neutralization

Neutralization of antimicrobials by adsorbent polymeric beads varies depending upon dosage level and timing of specimen collection. Internal studies have demonstrated that antimicrobials are effectively neutralized by the BacT/ALERT FA Plus medium. In these tests, antimicrobials were added in clinically relevant concentrations directly to culture bottles during inoculation with susceptible strains. The effectiveness of the antimicrobials was confirmed by parallel testing using a non-neutralizing medium as a control. Antimicrobials from the following antimicrobial/antimicrobial categories were neutralized by the medium: penicillins, glycylcyclines, polyenes, macrolides, triazoles, echinocandins, cefazolin, cefoxitin, cefotaxime, ceftaroline , aminoglycosides, fluoroquinolones, lincosamides, glycopeptides, and oxazolidinones.

Antimicrobial neutralization was not achieved for ceftazidime or cefepime.

Less than complete neutralization was observed for cefotaxime and ceftriaxone. Cefotaxime was neutralized at ranges of 50% PSL to 2% PSL depending on the microorganism. Ceftriaxone was neutralized at ranges of 50% PSL to 1% PSL depending on the organism. For additional information on antimicrobial agents neutralized by FA Plus bottles, contact your local bioMerieux representative.

Potentially Interfering Substances

In-house seeded studies were conducted with cerebrospinal fluid, pleural fluid, synovial fluid, plasma, blood, and blood clots. Aliquots of each of these fluids also received white blood cells at concentrations relevant to bacteremia in each given body fluid. Testing was conducted with and without microorganisms. These substances neither interfered with recovery and detection of organisms, nor did they generate false positive results in the absence of organisms.

Limit of Detection (LoD)

Data shows results from in-house seeded studies. A minimum of 30 replicates were tested per species. The data was generated using bottles at end of shelf life. Bottles inoculated with *H. influenzae* received 4 ml pooled human blood supplementation. At least 95% detection was achieved at LoD.

Table 3. Table 2 Summary of LoD Data

Microorganism	Strain ID	LoD (CFU/bottle)
Candida albicans	ATCC 14053	6
Enterobacter aerogenes	ATCC 13048	8
Enterococcus faecalis	NCTC 12697	5
Escherichia coli	NCTC 12923	4
Haemophilus influenzae	ATCC 10211	6
Klebsiella pneumoniae	STL 104016	4
Listeria monocytogenes	ATCC 15313	6
Pseudomonas aeruginosa	NCTC 12924	4
Salmonella enterica	ATCC 14028	5
Staphylococcus aureus	NCTC 10788	5
Streptococcus pneumoniae	ATCC 6305	6

Within-Laboratory Precision (Repeatability)

Data represents results from in-house seeded studies conducted on 12 days on multiple instruments by multiple operators. Organisms were grown in the presence of clinically relevant concentrations of antimicrobials to which they are susceptible. In this seeded study BacT/ALERT FA Plus bottles were subcultured at least 24 hours after being flagged positive by the instrument. A minimum of 108 replicates were tested for each organism/antimicrobial combination.

Table 4. Summary of the Within-Laboratory Precision Data

Sample Input		CFU/bottle (range)	% Recovery				Time to Detection (hours)	
Organism	Antimicrobial		Lot 1	Lot 2	Lot 3	Overall	Mean	Range
C. albicans	Fluconazole	140 - 364	100.0	100.0	100.0	100.0	26.0	22.8 - 31.3
E. coli	Amikacin	26 - 156	100.0	100.0	100.0	100.0	12.0	11.2 - 13.0
K. pneumoniae	Levofloxacin	108 - 170	100.0	100.0	100.0	100.0	13.4	11.7 - 15.2
P. aeruginosa	Piperacillin	80 - 148	100.0	97.2	100.0	99.1	19.2	17.4 - 24.1
S. pneumoniae	Penicillin G	9 - 505	100.0	100.0	100.0	100.0	13.2	11.6 - 15.5
S. aureus	Vancomycin	94 - 158	100.0	100.0	100.0	100.0	16.9	14.6 - 20.3

Reproducibility

Data represents results from seeded studies conducted at three sites using a target of 162 replicates per site on 3 days with a minimum of two operators per site. Reproducibility was evaluated on each of 9 organisms. Two organisms (C. albicans and S .pneumoniae) were prepared via serial dilution and the other 7 organisms were prepared using BioBalls. C. albicans and S. pneumoniae were seeded into the FA Plus bottle, at a target inoculum of 100 CFU/bottle, with an

acceptable range of 30-300 CFU/bottle and the other 7 organisms at a target range of 1-17 CFU/bottle. The actual inoculum ranged from 6 CFU/bottle to 700 CFU/bottle for the 30-300 CFU/bottle range, and from 1 CFU/bottle to 270 CFU/bottle for the 1-17 CFU/bottle range. Percent recovery reflects positive flag by the instrument and Gram-stain/subculture consistent with the seeded organism.

Table 5. Summary of Reproducibility Data

Sample Input	% Recovery				Time to Detection		Inoculum Ranges (CFU/Bottle)
	Site 1	Site 2	Site 3	Overall	Mean	Range	
S. aureus	100.0% (18/18)	87.5% (21/24)	100.0% (30/30)	95.8% (69/72)	15.6	14.6-16.7	2-11
C. albicans	100.0% (18/18)	83.3% (30/36)	100.0% (33/33)	93.1% (81/87)	36.6	24.6-76.8	14-700
E. coli	100.0% (27/27)	77.8% (21/27)	100.0% (30/30)	92.9% (78/84)	12.8	11.8-14.1	1-38
P. aeruginosa	100.0% (24/24)	75.0% (18/24)	97.0% (32/33)	91.4% (74/81)	18.4	17.1-21.1	1-11
E. faecalis	100.0% (18/18)	79.2% (19/24)	96.7% (29/30)	91.7% (66/72)	13.9	12.6-15.3	1-15
E. aerogenes	74.4% (29/39)	72.2% (26/36)	85.4% (41/48)	78.1% (96/123)	14.9	11.7-20.8	1-270
L. monocytogenes	100.0% (18/18)	100.0% (24/24)	100.0% (30/30)	100.0% (72/72)	24.1	20.4-36.4	1-14
S. enterica	100.0% (24/24)	75.0% (18/24)	100.0% (33/33)	92.6% (75/81)	13.5	2.3-14.8	1-13
S. pneumoniae	100.0% (30/30)	100.0% (36/36)	100.0% (21/21)	100.0% (87/87)	14.2	11.6-18.9	6-500
Overall	**95.4% (206/216) 95% CI: 91.7%, 97.8%**	**83.5% (213/255) 95% CI: 78.4%, 87.9%**	**96.9% (279/288) 95% CI: 94.2%, 98.6%**	**92.0% (698/759) 95% CI: 89.8%, 93.8%**			

The above data includes repeat testing performed as a result of laboratory errors at a single site (i.e. contaminated bottles/reagents, colony counts out of range, and site failure to change bottle status after positive instrument signal and positive subculture). Data excluding the laboratory errors demonstrated 100% recovery with the exception of *E. aerogenes*, which exhibited 85.0% recovery for all sites combined.

Delayed Entry

Results from seeded studies using 11 species* at target concentrations 100 CFU per bottle (acceptable range of 30 to 300 CFU per bottle) were generated at three sites. Actual inoculum levels ranged from 35 CFU/bottle to 290 CFU/bottle. All bottles contained human blood from healthy volunteers and were held at specified temperatures and times prior to loading into the BacT/ALERT instrument. Percent recovery reflects positive flag by the instrument and Gram stain/subculture consistent with the seeded organism.

Table 6. Summary of Delayed Entry Data

Sample Input	Incubation Temperature (°C)	Hold Time (hours)	% Recovery	Time to Detection from Sample Inoculation (Hold Time + Instrument TTD in hours)	
				Mean	Range
Inoculated Test Bottles	Control	No delay	100.0% (459/459)	14.3	8.5 - 84.0
	2-8	48	98.6% (292/296)	63.7	57.5 - 103.2
	20-25	24	98.0% (291/297)	31.8	26.2 - 74.4
	20-25	36	91.9% (272/296)	41.8	38.0 - 70.5
	35-37	8	98.9% (454/459)	16.1	10.2 - 53.8
	35-37	24	56.6% *** (259/458)	28.3	26.0 - 74.4
Negative Controls	All conditions		0.5% (1/221)**	-	-

**Staphylococcus aureus, Candida albicans, Candida krusei, Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Streptococcus pneumoniae, Enterococcus faecium, Haemophilus influenzae, Neisseria meningitidis*

**False positive observed during seeded study (1/221)

*** CAUTION: Culture bottles held at 35 to 37°C for 24 hours or longer before loading may not detect microorganisms and should be subcultured.

Clinical Study Results (Blood Cultures)

A multi-center clinical study was conducted at three different geographic sites in the U.S. comparing the performance of the FA Plus and FA blood culture bottles for aerobic culture pairs that received blood volumes between 6 ml and 10 ml (compliant pairs). A total of 1656 bottle pairs were obtained from 728 adult patients suspected of blood stream bacterial/yeast infections. Subcultures of both bottles were performed when either bottle in the set was determined to be positive by the BacT/ALERT system. A pair of bottles was determined to have a positive status if the subculture of either the FA Plus or FA bottle was positive. A culture bottle was determined to be a "True Positive" if the culture was flagged positive by the BacT/ALERT System and resulted in growth of the isolate upon subculture of this bottle. True positive rates were calculated for the FA Plus and FA culture bottles, and the ratio of FA Plus true positives to FA true positives was calculated to compare performance. Clinical isolates recovered were classified as significant, contaminant, or unknown based on determination by the clinical trial sites.

A total of 267 isolates were recovered from all compliant aerobic culture pairs with a positive status. There were a total of 238 bottle pairs that recovered at least 1 isolate by subculture of FA Plus or FA bottles. A total of 214 bottle pairs recovered a single isolate, 19 bottle pairs recovered two isolates, and 5 bottle pairs recovered 3 isolates. The total population reported in table below comprises the 267 isolates recovered from positive bottle pairs and 1418 negative bottle pairs for a total of 1685 results.

The BacT/ALERT FA Plus bottle detected a total of 208 isolates compared to the BacT/ALERT FA bottle that detected 194 isolates. Of the significant isolates, the BacT/ALERT FA Plus bottle detected a total of 159 isolates compared to the BacT/ALERT FA bottle that detected 135 isolates. Five false positives were identified by subculture of positive BacT/ALERT FA Plus bottles and comprised 0.30% (5/1685) of the study population.

Table 7. All Compliant Pairs with Single and Multiple Isolates Combined (Blood Cultures)

Clinical Isolate Determination	BacT/ALERT FA Plus True Positives	% of BacT/ALERT FA Plus True Positives in Population	BacT/ALERT FA True Positives	% of BacT/ALERT FA True Positives in Population	Ratio of True Positives*
Significant	159	9.4% (159/1685)	135	8.0% (135/1685)	1.178
Contaminant	36	2.1% (36/1685)	47	2.8% (47/1685)	0.766
Unknown	13	0.8% (13/1685)	12	0.7% (12/1685)	1.083
Total	*208*	*12.3% (208/1685)*	*194*	*11.5% (194/1685)*	1.072

*Sixty (60) isolates were detected by both FA Plus and FA, 25 isolates were detected only by FA Plus and 7 isolates were detected only by FA. The ratio of true positive rates for overall isolates was 1.072 (208/194) with a 95% CI of (0.952, 1.193).

Clinical Study Results (Sterile Body Fluid Cultures)

A multi-center clinical study was conducted at four different geographic sites in the U.S. and Canada comparing the performance of the FA Plus and FA culture bottles with sterile body fluid specimens (SBF). A total of 404 bottle pairs were obtained from 369 adult patients suspected of SBF bacterial/yeast infections. Sterile body fluid types evaluated were amniotic fluid, continuous ambulatory peritoneal dialysis (CAPD) fluid, cerebrospinal fluid (CSF), peritoneal fluid, pleural fluid, and synovial fluid. Clinical isolates recovered were classified as significant, contaminant, or unknown based on determination by the clinical trial sites.

A total of 92 isolates were recovered from all aerobic SBF culture pairs with a positive status. There were a total of 75 bottle pairs that recovered at least 1 isolate by subculture of FA Plus or FA bottles. A total of 62 bottle pairs recovered a single isolate, 9 bottle pairs recovered two isolates, and 4 bottle pairs recovered 3 isolates. The total population reported in table below comprises the 92 isolates recovered from positive bottle pairs and 329 negative bottle pairs for a total of 421 results. The FA Plus bottle detected a total of 85 isolates compared to the FA bottle that detected 67 isolates. Of the significant isolates, the FA Plus bottle detected a total of 65 isolates compared to the FA bottle that detected 59 isolates. No false positives were observed for the FA Plus bottle from the study population (0/421).

Table 8. All Pairs with Single and Multiple Isolates Combined (Sterile Body Fluids)

Clinical Isolate Determination	BacT/ALERT FA Plus True Positives	% of BacT/ALERT FA Plus True Positives in Population	BacT/ALERT FA True Positives	% of BacT/ALERT FA True Positives in Population	Ratio of True Positives*
Significant	65	15.4% (65/421)	59	14.0% (59/421)	1.102
Contaminant	13	3.1% (13/421)	2	0.5% (2/421)	6.500
Unknown	7	1.7% (7/421)	6	1.4% (6/421)	1.167
Total	*85*	*20.2% (85/421)*	*67*	*15.9% (67/421)*	*1.269*

*Sixty (60) isolates were detected by both FA Plus and FA, 25 isolates were detected only by FA Plus and 7 isolates were detected by only FA. The ratio of true positive rates for overall isolates was 1.269 (85/69) with a 95% CI of (1.083, 1.455).

Proposed labeling

The proposed labeling is complete.

Conclusion

The information in this premarket notification is complete and supports a substantial equivalence decision.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

bioMerieux Inc.
C/O Jocelyn Jennings
Senior Manager, Regulatory Affairs
100 Rodolphe Street
Durham, NC 27712

JAN 2 2 2013

Re: k121461
Trade/Device Name: BacT/Alert FA Plus Culture Bottle
Regulation Number: 21 CFR 866.2560
Regulation Name: Microbial Growth Monitor
Regulatory Class: Class I
Product Code: MDB
Dated: January 14, 2013
Received: January 15, 2013

Dear Ms. Jennings:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

INTENDED USE STATEMENT

510(k) Number (if known): K121461

Device Name: BacT/ALERT® FA Plus Culture Bottles

Intended Use:

BacT/ALERT® FA Plus Culture Bottles are used with the BacT/ALERT® Microbial Detection System in qualitative procedures for recovery and detection of aerobic and facultative anaerobic microorganisms (bacteria and yeast) from blood and other normally sterile body fluids.

Prescription Use ___X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostics and Radiological Health

510(k) K121461